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Original Article

A Transcatheter Closure of Large-Size Patent Ductus Arteriosus with Severe Degree of Pulmonary Hypertension by Different Types of Devices

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ABSTRACT

Background: Transcatheter closure is the most common treatment for patent ductus arteriosus (PDA); however employing large PDA is difficult because there are few closure devices, and surgical treatment is risky, especially in young infants with low weight and adults with calcified PDA. This study examines transcatheter closure and pulmonary artery (PA) pressure reversibility in large PDA with severe pulmonary hypertension.

Methods: A prospective research examined high PA pressure in 34 patients with big PDA and severe pulmonary hypertension (PHT) who were closed with various occludes. Clinical and transthoracic echocardiographic follow-up at 4 weeks, 3 months, 6 months, and 12 months post-closure measured PA pressure and closure effectiveness.

Results: In total, 34 big PDAs with significant PHT were transcatheter-closed in 723 individuals. Patients were from a few months old to adults and weighed from 4.25 to 61kg, which were tested by using ADO1, MVSD, AVP2, ASDO, and a stent-closed PDAs. After the intervention, the PA systolic, mean, and diastolic pressures were 36.85±11.12mmHg, 29.24±10.09mmHg, and 23.35±8.82 mmHg, respectively. Moreover, after the intervention, the aortic systolic, mean, and diastolic pressures were 112.38±16.97mmHg, 76.00±9.73mmHg, and 61.88±8.73mmHg, respectively. Two instances showed rebound PA pressure 3 months after effective treatments that did not respond to pulmonary vasodilator therapy. The median size of PDA in 10 cases closed by MVSD was 11.59±3.15mm, and the device size was 16.20±3.46mm; moreover, the defect size in 15 cases closed with ADO I device was 9.19±3.46mm, and the median size of occluder was 11.07±4.06mm. In 4 cases, the median size was 5.15±0.65mm, mostly in infants closed by an AVP2 occluder with a device size of 8.50±1.00mm.

Conclusion: Transcatheter closure of large PDA with severe PHT using the off-labeled device is feasible and effective. Meticulous and continuous assessment and evaluation of PHT response for closure is mandatory to confirm longstanding efficacy and safety.

Keywords: Ductus arteriosus patent, Pulmonary hypertension, Transcatheter, Vascular closure devices

Introduction

Patent ductus arteriosus (PDA) is a prevalent congenital heart defect, accounting for approximately 10% of all congenital heart diseases (1, 2). This condition occurs more frequently in females, with a female-to-male incidence ratio of nearly 2:1 (1, 2). The PDA originates from the left sixth aortic arch and connects the descending aorta to the main pulmonary artery. After birth, the contraction of the PDA's medial smooth muscle leads to constriction, functional closure, and eventually permanent closure, forming the ligamentum

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arteriosum (3). Failure of duct constriction results in persistent ductal patency. In 1967, Porstmann et al. conducted the first percutaneous closure of a PDA using a preshaped Ivalon plug (4). PDAs exhibit various shapes; however, most commonly, the aortic end is wide, narrowing towards the pulmonary end (5).

Jacobs et al. classified PDAs into five types based on their morphological features (6). Transcatheter PDA closure using different coils and devices has become an established alternative to surgical closure, particularly for non-complicated PDAs in infants and older children, with high success rates and low risk of complications (7). The management of large PDAs with severe pulmonary hypertension (PHT) in adults and older children presents a challenge to surgeons and interventional cardiologists (8). Potential complications include device embolization, residual shunt, ductal rupture, and aortic and/or pulmonary obstruction (9). It is crucial to confirm the reversibility of the pulmonary vascular bed before proceeding with duct closure (10). This study aimed to assess the feasibility of transcatheter closure and analyze the reversibility of PA pressure in large-size PDA with severe PHT.

Methods

From October 2011 to August 2022, 723 patients underwent transcatheter closure of PDA of them 34 cases with large-size PDA and severe degree of PHT underwent successful transcatheter closure. The patients were selected from those who visited outpatient clinics and diagnosed by clinical and echocardiography evaluation. There are different clinical and investigational methods used for assessing pulmonary vascular resistance reversibility, including upper and lower limb Spao2 saturation at rest and after exercise, chest X-ray, electrocardiogram, transthoracic echocardiography, and cardiac catheterization. Findings that were considered features of irreversible pulmonary vascular resistance were Spao2 before or after exercise below 93%, lack of left heart side dilatation and increase pulmonary vascularity on chest X-ray, lack of left ventricular (LV) force dominancy on electrocardiogram and bidirectional or dominant right to left shunting with absence of LV volume overload on echocardiography in comparison, Spo2 constantly above 93%, increased pulmonary vascular marking with LV configuration cardiomegaly, and increased LV forces and dominant left to right shunting at PDA.

In cardiac catheterization when the systolic pulmonary artery pressure should be two thirds of the systolic aortic pressure with a ratio of pulmonary (QP), the systemic flow (QS) is greater than 1.5:1.0. Any patients that show irreversibility were excluded from the study. Informed consent was obtained, and under general anesthesia, in cardiac catheterization, a 4, 5, or 6 F sheath for the femoral artery and 5, 6, or 7 F sheath for the femoral vein were obtained. Oxygen saturation and pressure from different cardiac chambers were collected before and after 100% O2 administration. A descending aorta angiogram in left lateral and 30-degree right oblique projection to assess the size and anatomy of PDA was performed. The type and the size of the occluder were chosen according to the shape and size of the PDA, as well as the age and weight of the patient. The type of occluder was PDA occluder type 1, muscular Ventricular Septal Defect (VSD) occluder, Atrial Septal Defect (ASD) occluder, or vascular plug (These devices were either AGA medical corporation, Plymouth, MN, USA or Lifetech Scientific Ltd, Shenzhen, China).

When PDA is associated with Coarctation of the Aorta (COA) in small children, we dilate the COA and close the PDA in one session, while in adolescents and adults with severe COA and large PDA, we used covered CP stenting to relieve the COA and closing the PDA in the same time. Typically, occluders used in infants and young children are 1-3mm larger than the narrowest PDA size, while in older children, they are 2-4mm larger. A 5 or 6 F multipurpose catheter is advanced from the femoral vein to the PA, where the catheter crosses the PDA to the descending aorta and is replaced by an Amplatzer guide wire (260cm*0.35mm) to advance the delivery sheath. The size of the chosen device is 1-2mm in infants and 3-4mm in older patients larger than the narrowest PDA diameter measured angiographically. An angiogram is done by the delivery system in 35*35 LAO cranial to assess for any LPA obstruction and a descending aorta angiogram is to rule out residual shunt and descending aorta obstruction. Reversibility of PA pressure was considered if the systolic PA pressure decreased by 1/3 of systolic aortic pressure, and the aortic pressure either did not change or increase after 15 min of complete closure.

If there is COA and large size PDA, a Covered CP stent that covers the total coarctation segment and aortic ampulla of PDA was used. After the completion of the procedure, the patients were sent to the intensive cardiac unit with continuous monitoring of vital signs and oxygen saturation and

were rechecked by echocardiography the next day to assess occluder position, residual shunt, ventricular function, and pulmonary artery pressure (estimated by the degree of tricuspid regurgitation).

All patients were kept on anti-pulmonary hypertension medication with sildenafil and Bosentan during follow-up period (months to years) with serial follow-up at 1 month, 3, and 6 months, then every year looking for any evidence of exaggeration of pulmonary hypertension. Statistical analysis was carried out using SPSS software (version 27). Categorical variables were presented as frequencies and percentages. Continuous variables were presented as mean±SD. Paired t-test was used to compare means for two paired readings. A *P*-value of ≤ 0.05 was considered as significant.

Ethical approval

The study was initiated after obtaining approval from the institutional ethics committee in Babylon University , code of ethics: 1232 In 1/4/2022.

Results

In total, 34 patients with large PDA and severe PHT were included in this study. On the other hand, the patients with severe PHT and right to left shunt, Spo2 below 95% at rest, or Spao2 in the lower limb below 90% after exercise were excluded from the study. The patients were divided into 5 groups according to age; those below 5 years were 15 cases (44.2%), 5-10 years were 6 cases (17.6%), 10-15 years were 3 cases (8.8%), 15-20 years were 5 cases (14.7%), and above 20 years were 5 cases (14.7%). The majority of cases were female (n=23, 67.6%). The patients' weight range was from 4.25 to 61 kg (Table 1). The associated lesion is either corrected in the same session like the coarctation of the aorta or the latterm, except for MR which improved later when the left ventricle size returned to normal.

Table 1. The distribution of patients according to socio-demographic characteristics (n=34)

Weight (Kg)	(21.69±19.12)	(4.25-61.00)
Age (years)		
< 5 years	15	44.2%
5-10 years	6	17.6%
10-15 years	3	8.8%
15-20 years	5	14.7%
≥ 20 years	5	14.7%
Total	34	100.0%
Gender		
Male	11	32.4%
Female	23	67.6%
Total	34	100.0%

Cardiac catheterization

The PA systolic, mean, and diastolic pressure before intervention were 63.65±10.71 mmHg, 53.62±10.31 mmHg, and 43.94±9.46 mmHg, and after intervention, they were 36.85±11.12 mmHg, 29.24±10.09 mmHg, 23.35±8.82 mmHg, respectively. There is a significant decrease in PA pressures after occlusions. On the other hand, the aortic systolic, mean, and diastolic pressure before intervention were 103.21±30mmHg, 67, 67.24±12.60 mmHg, and 55.24±12.34mmHg, and after intervention, they were 112.38±16.97 mmHg, 76.00±9.73mmHg, and 61.88±8.73 mmHg, respectively, with documented increase of aortic pressure after occlusions. The most common type of occluder used was ADO1 in 15 cases (44.1%), with the most common size being 10/8mm in 8 cases (53.4%), and muscular VSD occluder (MVSD) in 10 cases (29.4%) with the most common size being 14mm in 3 cases (30%). Both the stent and vascular plug were used in 4 cases (11.8%), the 8mm vascular plug was used in 3 cases (75%), and stent size was 34mm and 39mm over 20mm BIB balloon and 34mm over 18mm and 22mm BIB balloon. The ASD occluder (14mm Amplatzer ASD occluder) was used in 1 case (Table 2, Figure 1). Complete closure without

Table 2. Distribution of patients according to size and type of occluder (n=34)

Type of occluder	Number	%
ADO1		
10/8 mm	8	53.4%
12/10 mm	2	13.3%
16/ 14 mm	1	6.7%
18/16 mm	2	13.3%
20/18 mm	2	13.3%
Total	15	100.0%
MVSD		
10 mm	1	10.0%
14 mm	3	30.0%
16 mm	2	20.0%
18 mm	2	20.0%
20 mm	1	10.0%
22 mm	1	10.0%
Total	10	100.0%
Stent		
34/20 mm	1	25.0%
34/22 mm	1	25.0%
34/ 18 mm	1	25.0%
39/20 mm	1	25.0%
Total	4	100.0%
Vascular-plug		
8 mm	3	75.0%
10 mm	1	25.0%
Total	4	100.0%
ASD		
14mm	1	100.0%
Total	1	100.0%

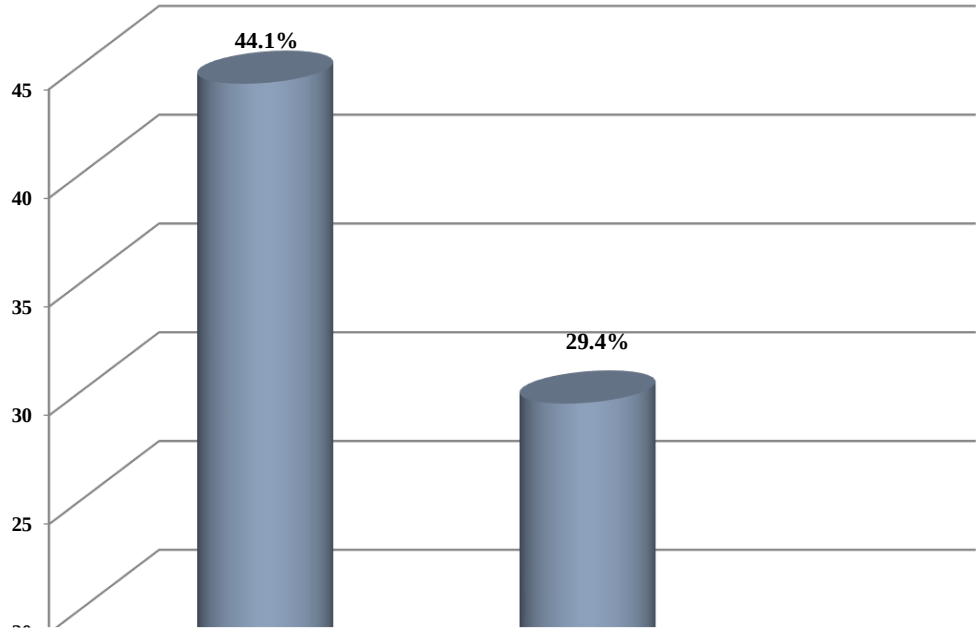

Figure 1. Distribution of patients according to the type of occluder (n=34)

residual shunt through the occluder was achieved in all cases, and complete occlusion of shunt and relief of COA was obtained through stent implantation.

The median size of PDA closed by MVSD was 11.59±3.15mm with a mean device size of 16.20±3.46mm. The defect size in 15 cases was 9.19×3.46mm, and the median size of the ADO1 occluder used to close these defects was 11.07×4.06mm. There were four cases in which the median size was 5.15×0.65mm, mostly infants with AVP2 occluders closing these defects, and the median size of the device used for closure was 8.50×1.00 mm, as shown in Figure 1.

There are different types of devices used for the closure of PDA, and the most widely used occluder is ADO1 in 15 cases (44.1%). Muscular VSD occluder (MVSD) was used in 10 (29.4%) patients. Stent and vascular plug were used in 4 (11.8%) patients, and ASD was used in 1 (2.9%) patient.

As presented in Table 3, in some cases, there are other congenital heart diseases associated with PDA in 12 cases (35.3%), and the coarctation of the aorta is the most widely disease.

The effects of pulmonary artery pressure and aortic pressure on mean pressure were presented

Table 3. The Distribution of patients according to other associated lesions (n=34)

Study variables	Number	%
Other associated lesions		
Present	12	35.3%
Absent	22	64.7%
Total	34	100.0%
Type of other associated lesions		
Coarctation of aorta	4	33.3%
Moderate MR	2	16.7%
Moderate size ASD secundum	3	25.0%
Small size VSD	3	25.0%
Total	12	100.0%

Table 4. The mean differences of pulmonary artery systolic, diastolic, and mean pressure (mmHg) before and after device occlusions (n=34)

Study variables	Periods of assessment	N	Mean±SD	Paired t-test	P-value
Pulmonary artery systolic pressure (mmHg)	Before balloon closure	34	63.65±10.71	21.556	<0.001*
	After balloon closure	34	36.85±11.12		
Pulmonary artery diastolic pressure (mmHg)	Before balloon closure	34	43.94±9.46	15.513	<0.001*
	After balloon closure	34	23.35±8.82		
Pulmonary artery mean pressure (mmHg)	Before balloon closure	34	53.62±10.31	17.839	<0.001*
	After balloon closure	34	29.24±10.09		

*P-value of ≤ 0.05 was significant.

Table 5. The mean differences of aortic systolic, diastolic, and mean pressure (mmHg) before and after device occlusion (n=34)

Study variables	Periods of assessment	N	Mean±SD	Paired t-test	P-value
Aortic systolic pressure (mmHg)	Before device occlusion	34	103.21±30.07	-2.693	0.011*
	After device occlusion	34	112.38±16.97		
Aortic diastolic pressure (mmHg)	Before device occlusion	34	55.24±12.34	-4.466	<0.001*
	After device occlusion	34	61.88±8.73		
Aortic mean pressure (mmHg)	Before device occlusion	34	67.24±12.60	-6.707	<0.001*
	After device occlusion	34	76.00±9.73		

*P-value of ≤ 0.05 was significant.

in Tables 4 and 5, respectively. It was found that balloon closure can reduce the pulmonary artery mean pressure by up to 45%, and the device occlusion can increase the aortic mean pressure by 12%.

The size effects interaction between PDA and occlude sizes are compared in Table 6. As shown in Table 6, a *P*-value of ≤ 0.05 was considered significant for the studied cases in this research.

Table 6. The mean differences between PDA size (mm) and occluder size (mm) among study patients

Type of occluder	Measurement (mm)	N	Mean±SD	Paired t-test	P-value
MVSD	PDA size	10	11.59±3.15	-21.68	<0.001*
	Occluder size	10	16.20±3.46		
ADO1	PDA size	15	9.19±3.46	-9.41	<0.001*
	Occluder size	15	11.07±4.06		
Vascular-plug	PDA size	4	5.15±0.65	-12.59	0.001*
	Occluder size	4	8.50±1.00		

*P-value of ≤ 0.05 was significant.

Discussion

This study assessed the application of device occlusion of large-size PDAs with severe PHT in different age groups using various devices. The current study included a wide range of ages, similar to the studies by Campanh et al. (3) and Khushal et al. (11). Hemodynamic assessment prior to closure decisions is crucial to exclude patients with irreversible pulmonary hypertension (4). Considering the lack of awareness and delay in diagnosis, patients with large PDA and severe PAH are usually detected in developing countries. Nonsurgical modalities for the large hypertensive ductus closure have been extensively substituted by surgical possibilities, significantly during neonatology (12, 13, 14). Children with high PA pressures and small left-to-right or bidirectional shunts must determine pulmonary vascular reactivity and reversibility, specifically in early steps to aid in the closure of the fault (15).

Temporary occlusion of the PDA is considered the best way to assess PA pressure and reversibility (10, 16). Vasodilators were used before and after intervention in our study (17). Different types of devices were used for PDA closure depending on factors, such as patient age, PDA size, anatomy, and associated lesions. ADO1 occluders were used in infants and young children (10, 18), while muscular VSD occluders were preferred in older patients with large PDAs and severe PHT (18). In cases with coarctation of the aorta, cover CP stents were used (19). ASD occluders were occasionally used for large PDAs (20), and Amplatzer vascular plug type 2 was used for infants weighing less than 6 kg (21). Yan et al. (21) also used devices instead of balloons for the occlusion of large PDAs in patients with borderline PA pressure, similar to our study.

Post-procedure pulmonary hypertension is defined when the systolic pulmonary artery pressure is greater than 50mmHg, which persists 6 months after closure (22). The success rate of PDA closure in our study was 100%, while other studies had lower success rates, such as studies by Zabal et al. (74%) (23), Khushal et al. (65%) (11), and Garcia-Montes et al. (18%) (24). The success rate depends on factors, such as interventional doctor experience, patient age and weight, PDA size and shape, and the degree of PA pressure (25).

Conclusion

Transcatheter closure of PDA is a safe and effective method, the availability of multiple types of devices used for the closure of large size PDA is the best way to avoid surgical intervention in

large-size PDA and severe degree of PHT. However, the device occlusion is a challenging method for assessing the reversible pulmonary artery pressure. Due to our limitations in hospital cases, we extracted statistical data from our case series study in one hospital; however, due to the time consumed, these analyses may be more reliable by doing the research in parallel hospitals.

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None.

Conflicts of interest

The authors declare that there is no conflict of interest.

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